

From Page No.

I was asked to find a way to further solubilize CoQ10 than the ~5% that theoretically could be obtained in soybean oil, and to use some kind of co-solvent if needed. My first guess was to solubilize it in D-Limonene, because it acts like a total solvent with beeswax — you need ≥10% beeswax in formulations that have a high limonene content because it just dissolves the beeswax but it wasn't there. So I took 50g of D-Limonene and started stirring in CoQ10, one or two grams at a time, by hand, and at room temperature. I stopped at 40% CoQ10 (20 grams in 50g D-Limonene), although I could have dissolved more in there. After about 30% or so, the solution starts to get a little cloudy after adding the CoQ10, but with 1-3 minutes of steady, slow stirring with the glass rod the CoQ10 completely dissolves and the solution clears up. After getting a clear, dark red 40% solution of CoQ10 in D-Limonene, I wanted to see what would happen when the solution was added to oil, since pure D-Limonene isn't really practical for a softgel fill — although we do make such a oil — 1 or 2% at a time — and I ended up adding the entire amount of CoQ10 solution to the soybean oil. It resulted in a clear, dark red solution, with no precipitation or phase separation at all — we'll see how it is after some time passes, although I don't expect anything bad to occur at all. The final soybean oil/D-Limonene/CoQ10 overall is 20% of CoQ10 that is completely solubilized.

3/17

The 20% CoQ10 in 50:50 Soybean oil/D-Limonene shows ~1-2% precipitation out over the weekend (~1 gram).

The trial that I added 10% D-Limonene shows the same amount of 2 powder at the bottom as on Friday, which is mostly or all a top layer.

The one with 10% glycerin still has the glycerin at the bottom, separated, but no other precipitate is evident.

The one with 10% vitamin E shows a dark (amber-brown) when I first added it, which it still is, but no precipitation.

The one I added 10% water to precipitated a very small amount at the interface.

The one with 10% lecithin shows no separation or precipitation.

Next I am going to try and make a solubilized CoQ10 in limonene solution and then combine it with some CoQ10 formulations with oil.

Witnessed & Understood by me,

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3/14/83

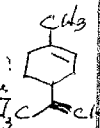
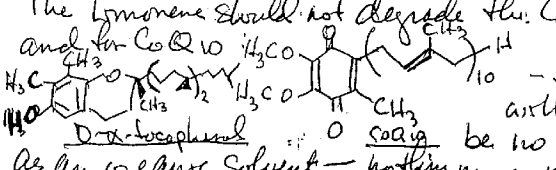
To Page No. 145

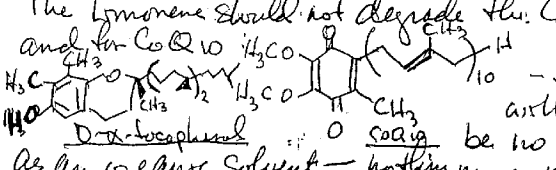
From Page No. 144 Any beeswax and see how it comes out and how it behaves after some time passes. The formula for CC-930 (CoQ10 100 mg) is:

Co-FA-MX-00016	Cocoyne <u>Q10</u>	104.0900 mg	100 grams
VI-FA-MX-00191	4-SO med Tocopherols 32 mg	269.0300 mg	.45 g
RE-FF-MX-00077	Rice Bran Oil	176.0200 mg	.35 g
BE-PA-MX-00053	Yellow Beeswax	20.0000 mg	10.52 g
BE-FA-MX-00203	Natural Beta Carotene 255,800 mg	10.0500 mg	3.45 g
		580.0000 mg	1.73 g

I'm going to try, first of all, to remove the Beeswax and the Rice Bran Oil and dissolving the CoQ10 in the same amount of Limonene that would be the weight of the RBO and beeswax, together (196.0200 mg/eq), so there'll be enough to dissolve it, then add the Vitamin E & Beta Carotene. Hopefully, the Vitamin E will help to keep the CoQ10 dissolved. Also the trial in the small vial I did on Friday maybe I'll keep the Beta Carotene out of the formula so I can see it for a few days - then add it. Anyway here is the formula I will use:

Cocoyne <u>Q10</u>	104.0900 mg	100 grams
4-SO med Tocopherols	269.0300 mg	77.95 g
D-Limonene	196.0200 mg	46.38 g
Natural Beta Carotene	10.0500 mg	33.97 g
	580.0000 mg	1.73 g

The Limonene should not degrade the CoQ10, as the similar Limonene  and for CoQ10  - there is nothing there that will react with either, so there should be no problem - the Limonene is just acting as an organic solvent - nothing more, nothing less.

Wow! As soon as you add the Vitamin E to it (and it's very light-colored Vitamin E) it turns a dark purple color! I hope it's just due to a change in oxidation state of one or both the Vitamin E and CoQ10 - there isn't anything that should react to change the structure of anything there. Had some CoQ10  but this same amt of Vit E in the other one - no discoloration. It looks good, I'm having assays done to see if anything happened.

Actually, looking at it, I can tell what To Page No. 146

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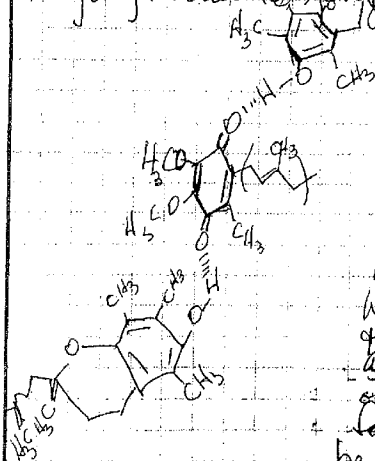
3/17/03

From Page No. 145

happened. The fully oxidized ketone groups on the quinone moiety of the Colloidal oxidized the hydroxyl group of the chromenol on the D-α-tocopherol, becoming a semi-quinone. Since the Colloidal is fully solubilized and the two molecules are in a compatible solvent, this would happen easily. There is nothing in any of the three molecules that could do anything else (no bonds broken, no ~~active~~ active hydrogen or alkali or anything) — there has just been a change in the oxidation states and the solution absorbs light at a different wavelength, that's all — in fact, it would make both molecules more like their active states, anyway. A similar thing happens to the Shalee Colloidal product in the gelatin — it darkens from an orange color to a deep brick red as the Colloidal becomes more solubilized and reacts with the Vitamin E in the product. It doesn't gel as easily as the because 1) there isn't as much Vitamin E in the Shalee product, and 2) the Colloidal doesn't solubilize as much in the Shalee product — both things happen here, and all the constituents are just as active as they should be.

The mixture that I made last night with less than in the place of the Vitamin E looked real good last night, but was very precipitated today — no good. I'm really encouraged with this project, though.

Thinking more on the interaction between the Colloidal and Vitamin E, it may only be due to hydrogen bonding between the molecules, like this:



Even if the two molecules were, in fact, causing partial oxidation state changes in each other, or if they were hydrogen bonding, either one is fine as far as their function and activity goes, and the only real change in them is not structural, or functional, so I don't see any problem here, other than maybe having to convince some of the less technical ones here about what, in fact, is happening and that the color change is nothing to worry about. Actually, if they are just changing the oxidation state of each other, that's all towards the more functional form of both molecules. It can only help — I'd be enormously surprised if it were anything else. I don't think anything is possible.

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To Page No. 147

3/1/03

TITLE Colloidal Solubility

From Page No. 146 When I added DL-tocopheryl acetate to the solubilized Colloidal solution there was no discoloration - it stayed the clear red color. But after sitting overnight there is a slight amount of precipitation on the bottom of the vial. There is also a slight amount of precipitation on the bottom of the vial & beaker with the D- α -tocopherol and the DL-tocopheryl acetate beaker - 33% Colloidal appears to be too concentrated - I'll have to bring it down to 30% or 28% and see how that does.

3/21/03

It's evident that the limonene is evaporating out of the open beakers, and that may be one of the reasons that I'm getting precipitation - although it is just a small amount (~1-2%). Here's an interesting note in the beaker that showed some precipitation after a day of sitting out - lost more limonene overnight on the second night, but the small amount of precipitation that formed the day before re-solubilized spontaneously. The only thing that I can think of that may be changing this is that over the 48 hours or so that the Colloidal was in the limonene, it needed that much time for a small amount of limonene to completely solubilize an even larger amount of Colloidal - it sounds a bit confusing, but I can't think of any other reason for this happening.

As for the assay I requested on the mix I made that was comparable to our CC-930 100% Colloidal solution - it came out well - the Colloidal was 110% of claim and the Vitamin E (mixed tocopherols) came out with good results for the separate components; in fact the gamma-tocopherol peak was as high as the D- α peak for our Chem 4-50 Vitamin E. There were no unexpected peaks in either assay so it proves my claim that the limonene doesn't hurt any of the substances and that the color change that occurs after adding the Vitamin E to the solubilized Colloidal is not due to anything other than a change in oxidation state. I'm very encouraged by all this, and am starting to hear exactly what they want me to do with it - there's a lot of possibilities ~~here~~ here, if we do it right.

3/26/03

Now I'm told to go ahead and try solubilizing 28-30% Colloidal in limonene, but they want me to add some color or something to it - just don't like the idea of so much limonene, although it won't hurt anything. The mix I made up before - off the 100% Colloidal product - the one that tested out so well, ended up with a small amount of crystals that formed on the bottom of the vial over time, so I'm convinced that the 33% is just too much for it - but adding all that much.

To Page No. 152

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3/19/03

From Page No. 141

Vitamin E - or anything else increases the chance that the Colloids will precipitate out - the one with 33% Colloids in Linnene and only 10% Vitamin E added, back on 3/14 still shows no precipitation, so that's encouraging, but I really don't think we need to add anything else, just the Colloids in Linnene - the Linnene won't hurt anything and it's already grand flavored in as a safe nutritional supplement to grade, so there's no regulatory problems with it.

End

TITLE TK-69

From Page No. 1

Sample of Linnene is the

AS-FA-MX-1
 VI-FA-MX-1
 VI-FA-MX-0
 VB-FA-MX-1
 VB-FA-MX-0
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To Page No. 11

Book 3

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